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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/623,458

07/17/2003

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EXAMINER

BABIC, CHRISTOPHER M

ART UNIT

PAPER NUMBER

1637

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/623,458	Applicant(s) GHARIZADEH, BABACK	
	Examiner CHRISTOPHER M. BABIC	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-12 and 17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-12 and 17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/11/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 11, 2008 has been entered. Claim(s) 1, 3-12, and 17 are pending.

Claim Objections - Withdrawn

The objection of claim(s) 2-12 has been withdrawn in view of Applicant's claim amendments.

Claim Rejections - 35 USC § 112 - Indefiniteness - Withdrawn

The rejection of claim(s) 2-12 is moot in view of the cancellation of claim 2. Thus, the rejection has been withdrawn.

Claim Rejections - 35 USC § 102 - Withdrawn

Applicant's claim amendments are sufficient to overcome the rejections of claims 2-5 over Tully and claims 1-5 over Ye. Tully and Ye are silent with regard to pyrosequencing. Thus, the rejections have been withdrawn.

Claim Rejections - 35 USC § 103 - Withdrawn

All previous rejections have been withdrawn for the reasons set forth above in section 35 USC 102.

Claim Rejections - 35 USC § 103 - New Grounds

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1. Claim(s) 1, 3-6, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alderborn et al. ("Determination of single-nucleotide polymorphisms by real-time pyrophosphate DNA sequencing." *Genome Res.* 2000 Aug;10(8):1249-58) in view of Ronaghi ("Improved performance of pyrosequencing using single-stranded DNA-binding protein." *Anal Biochem.* 2000 Nov 15;286(2):282-8), and in further view of Caskey et al. (U.S. 5,582,989).

With regard to claim 1, Alderborn teaches a determination of single-nucleotide polymorphisms (SNPs) by real-time pyrophosphate DNA sequencing (fig. 1; abstract, for example). Specifically, Alderborn teaches the providing of a sample containing

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target DNA with variable sequence regions (fig. 2-4; pg. 1257, DNA amplification, for example); providing sequencing primers and allowing such primers to hybridize to such DNA target (fig. 2-4; pg. 1257, annealing to identification oligonucleotide, for example); and sequencing such variable regions through pyrosequencing (fig. 2-4; pg. 1257, solid-phase pyrosequencing, for example).

Alderborn does not expressly teach providing a mixed pool of structurally different primers, each primer being specific for one species, group, or target, and mixing such mixed pool of primers with a target DNA; however, Alderborn expressly teaches identification of multiple different SNP sites on a single target DNA utilizing one primer (pg. 1253, teaches the primer elongation reaction proceeding over 18 bases of a template to elucidate two SNPs located 15 bases apart, for example). Thus, it was clear in the art at the time of invention that multiple SNP sites could be resolved in one reaction.

With regard to claim 17, Alderborn teaches pattern recognition (fig. 2-4, for example).

With regard to the use of two structurally different primer to resolve multiple SNP sites, it is first submitted that, as highlighted by Applicant on page 10 of Applicant's disclosure, at the time of invention the prior art recognized that pyrosequencing technology was limited to sequencing only short to medium sequence lengths, i.e. read length. Ronaghi provides a supportive disclosure that highlights the limited read length ability of the pyrosequencing method, even in the presence of a single stranded binding (SSB) protein, i.e. Ronaghi teaches that even after the addition of SSB, the

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pyrosequencing method only provides a read length of about 30 nucleotides (abstract; fig. 2, for example). Thus, it was clear in the art at the time of invention that the pyrosequencing method was limited to shorter sequence lengths.

In addition, the extension of multiple primers, each primer drawn to different target sequences, within the same reaction was a well known concept at the time of invention, i.e. multiplex extension. In particular, Caskey highlights the advantages of multiplexing nucleic acid amplification utilizing multiple structurally different primers, including the ability to detect multiple different separated target sequences, as well as the ability to detect multiple different loci of the same target sequence separated by large sequences in between the loci (col. 7, lines 20-55, for example).

With regard to claims 3 and 4, Caskey teaches multiple different target DNA from virus and bacteria (col. 5, lines 45-60, for example).

With regard to claims 5 and 6, Caskey teaches multiple different disease-linked variants (col. 7, lines 20-55, for example).

Thus, it was clear in the art at the time of invention that multiple different target sequences could be extended in a polymerase extension reaction.

In summary, it was clear in the art at the time of invention that the one primer within a pyrosequencing reaction would be unable to elucidate multiple SNP sites separated by large sequences (e.g. hundreds-thousands of nucleotides).

Thus, in summary, it is submitted that it would have been *prima facie* obvious to a skilled artisan at the time of invention to utilize multiple structurally different primers within the same reaction for detection of multiple different SNP sites separated by large

sequences, i.e. multiplex SNP detection, since the prior art demonstrates that such primers can extend different target loci separated by large sequences. A skilled artisan would have had a reasonable expectation of success with such a method since the prior art demonstrates that pyrosequencing can identify multiple different SNP sites within the same reaction.

2. Claim(s) 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alderborn et al. ("Determination of single-nucleotide polymorphisms by real-time pyrophosphate DNA sequencing." *Genome Res.* 2000 Aug;10(8):1249-58) in view of Ronaghi ("Improved performance of pyrosequencing using single-stranded DNA-binding protein." *Anal Biochem.* 2000 Nov 15;286(2):282-8), and in further view of Caskey et al. (U.S. 5,582,989) as applied to claim 6 above, and in further view of Rady et al. ("Type-specific primer-mediated direct sequencing of consensus primer-generated PCR amplicons of human papillomaviruses: a new approach for the simultaneous detection of multiple viral type infections. *J Virol Methods.* 1995 Jun;53(2-3):245-54").

The methods of the previously applied reference(s) have been outlined in the above rejections. The previously applied reference(s) do not expressly teach sequencing of HPV.

With regard to claim(s) 7-10, Rady provides a supporting disclosure that teaches the amplification of a conserved region within multiple different HPV types and

subsequent sequencing with sequence specific primers (page 246-249, materials and methods; fig. 1, for example).

With regard to claim(s) 11, the sequencing of low yield amplification of fragments is inherent to the methods of Ye.

Thus, in summary, it is submitted that it would have been *prima facie* obvious to a skilled artisan at the time of invention to utilize the methods suggested by the prior applied references to detect certain HPV types within a sample since the prior art demonstrates such methods as capable of identifying many different nucleic acid templates within the same reaction, thereby reducing the time needed for many separate reactions.

With regard to claim(s) 12, Caskey teaches the importance of designing primers that do not anneal to unspecific sequences (col. 4, lines 25-55, for example). Thus, it would have been *prima facie* obvious to a skilled artisan at the time of invention to design the multiplex sequencing primers such that they do not anneal to unspecific sequences and provide erroneous sequencing information.

Conclusion

Claim(s) 1, 3-12, and 17 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-

272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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